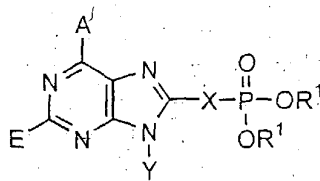


ABSTRACT

Novel purine compounds of the following structure and their use as fructose-1,6-bisphosphatase inhibitors is described.



wherein

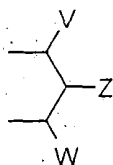
A is selected from the group consisting of $-NR^8$, $NHSO_2R^3$, $-OR^5$, $-SR^5$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, $-H$, and perhaloalkyl;

E is selected from the group consisting of $-H$, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, $-CN$, and $-NR^7$;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or together with Y forms a cyclic group including cyclic alkyl, heterocyclic, and aryl;

Y is selected from the group consisting of $-H$, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^1 is independently selected from the group consisting of $-H$, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$ -aryl, alkylaryl, $-C(R^2)_2OC(O)NR^2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, alkyl-S-C(O) R^3 , alkyl-S-S-alkylhydroxy, and alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alkyl-S-S-alkyl to form a cyclic group, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2_2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH}(\text{CH}=\text{CR}^2\text{R}^2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, and $-\text{R}^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-\text{R}^2$, then at least one of V and W is not -H or $-\text{R}^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-\text{C(O)R}^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidendate alkyl;

R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.